Supplementary Material

Synthesis of 2-heterosubstituted cyclopent-2-en-1-ones: a preliminary study of the strategic design of antiviral compounds

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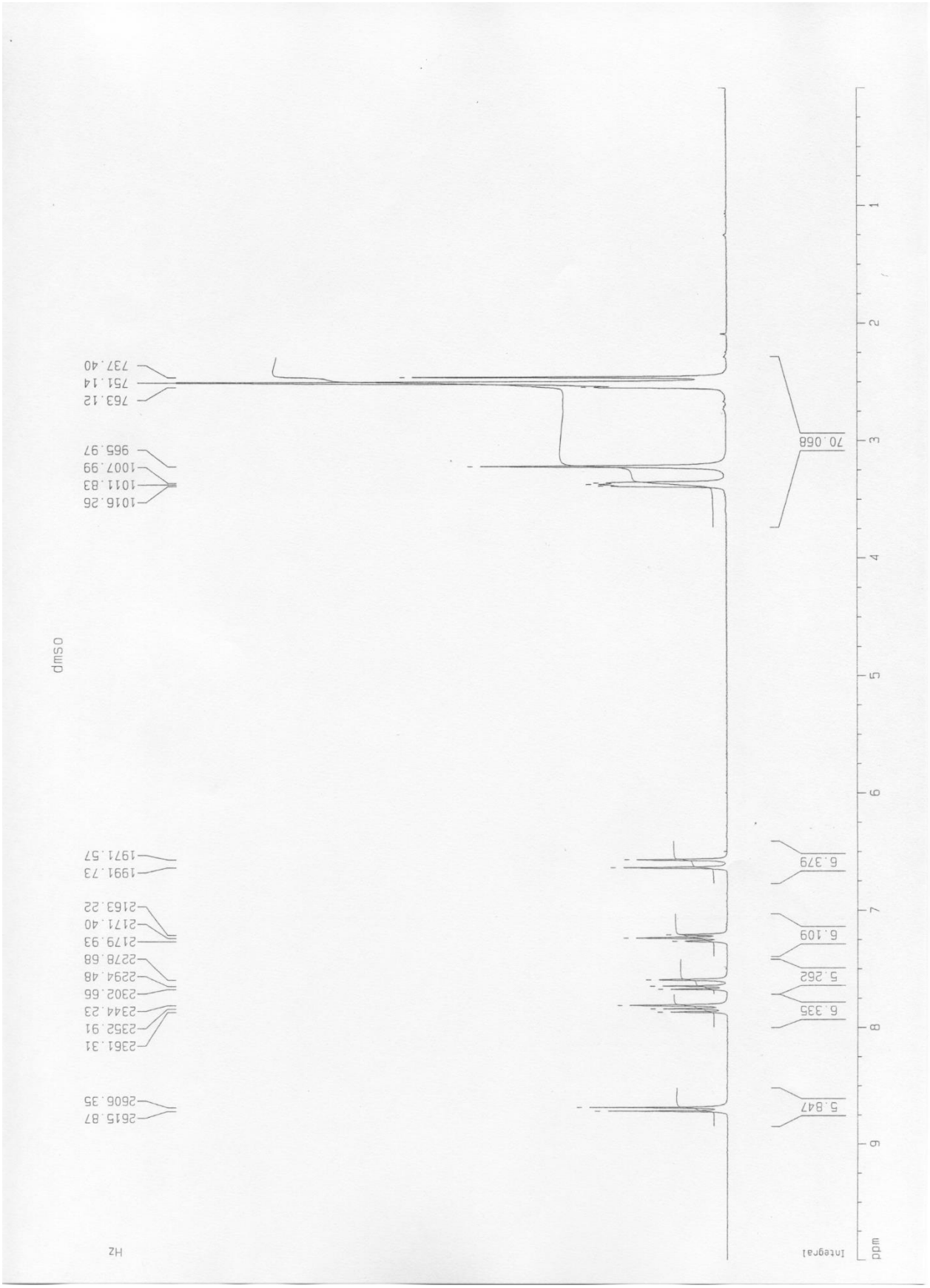
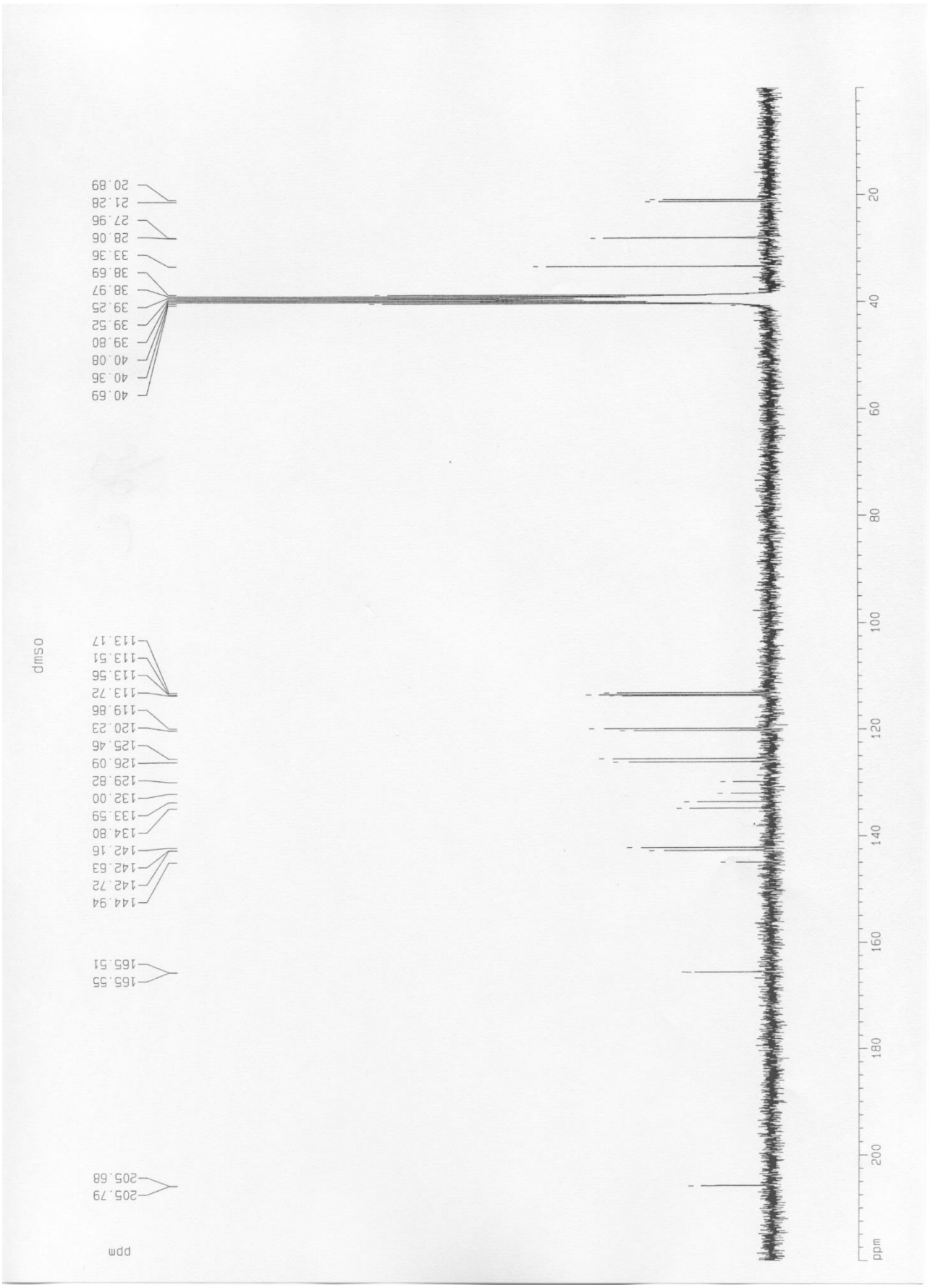
Table of Contents

Note: The NMR spectra here reported correspond to single crystallized compounds or crude compound as they were isolated from column chromatography. This was done to save precious pure samples for microanalyses and mainly for biological evaluations.

1. **^{1}H, ^{13}C, COSY and NOESY NMR spectra of new compounds**

5/6a





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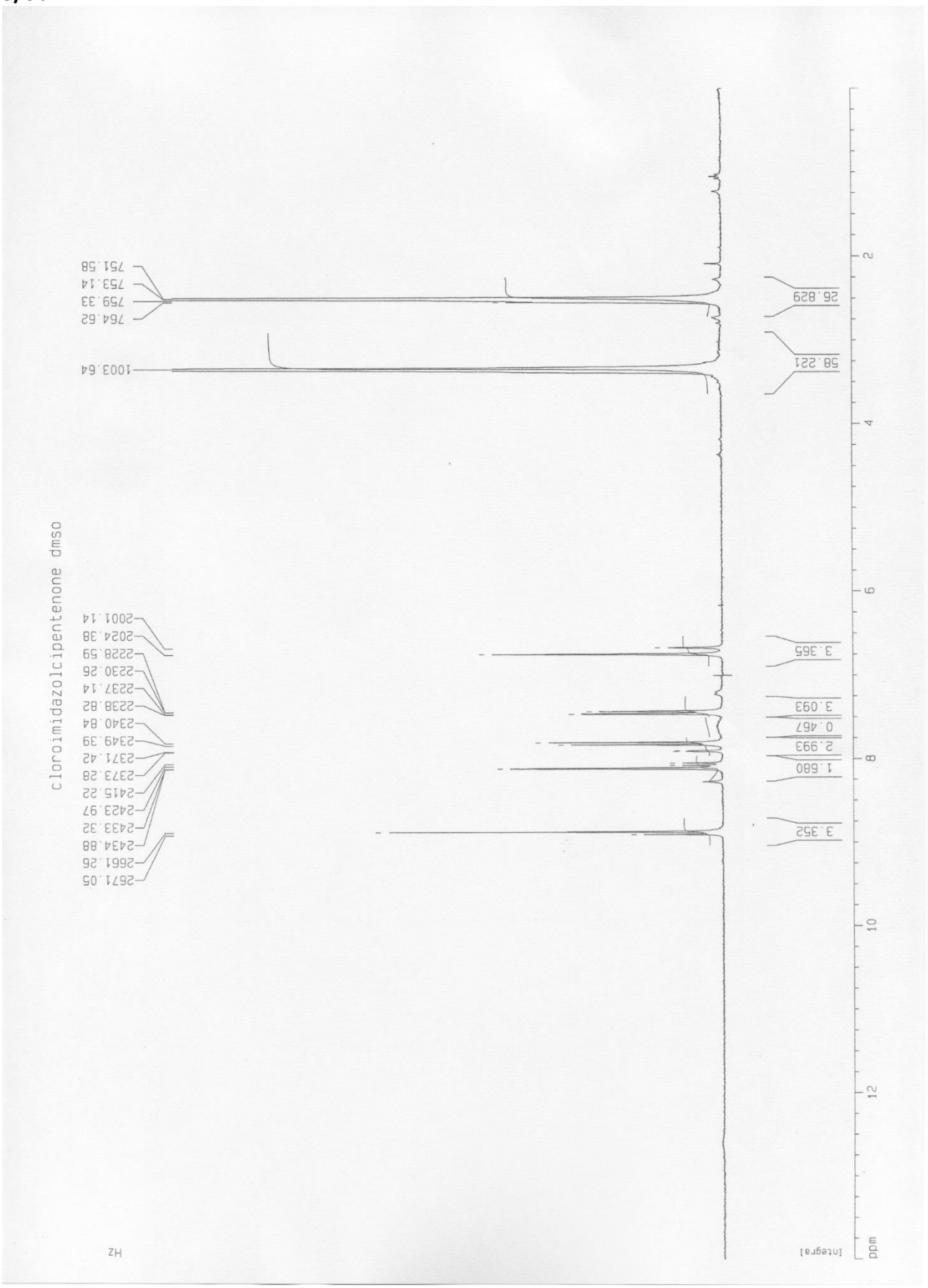

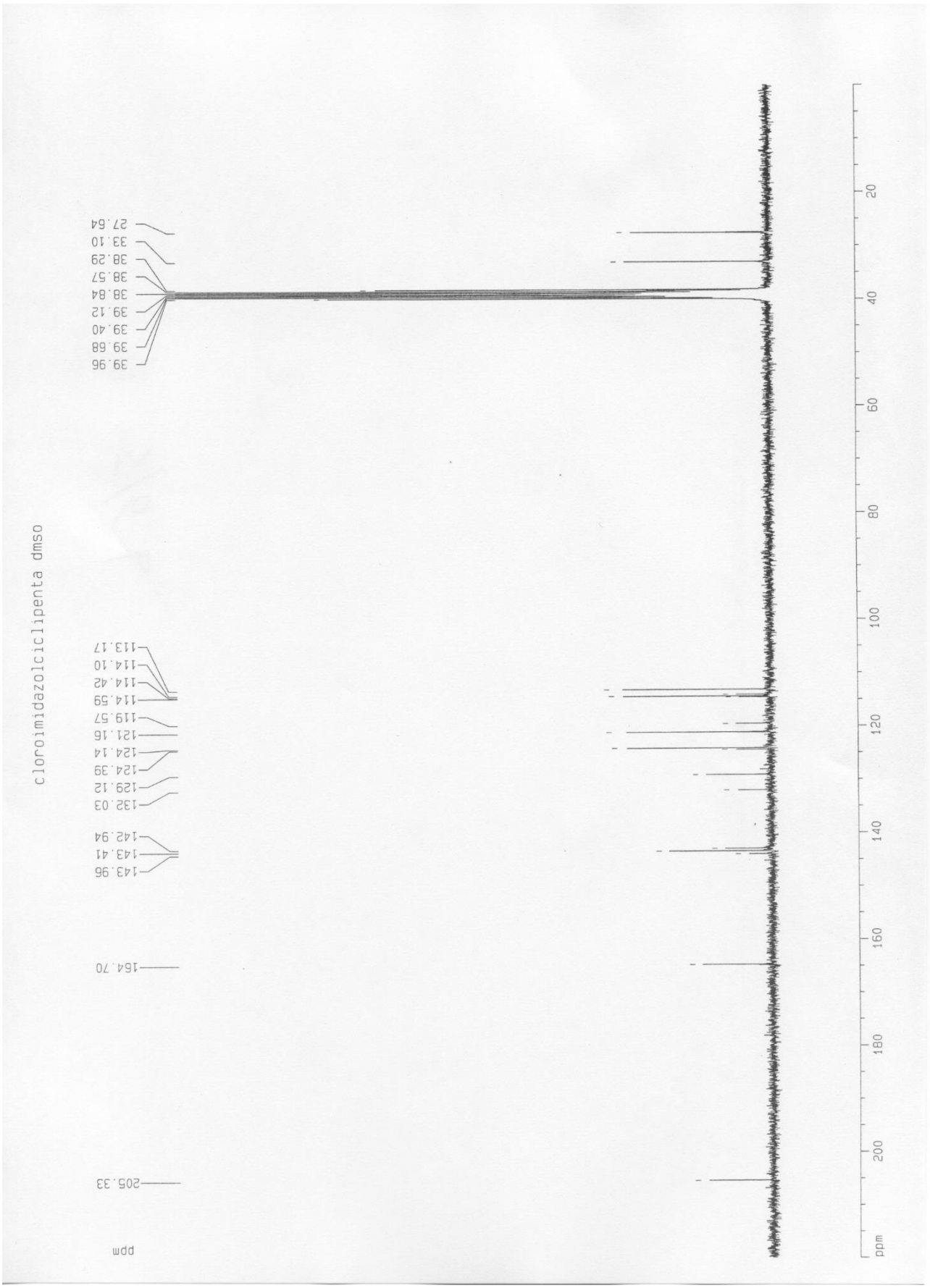

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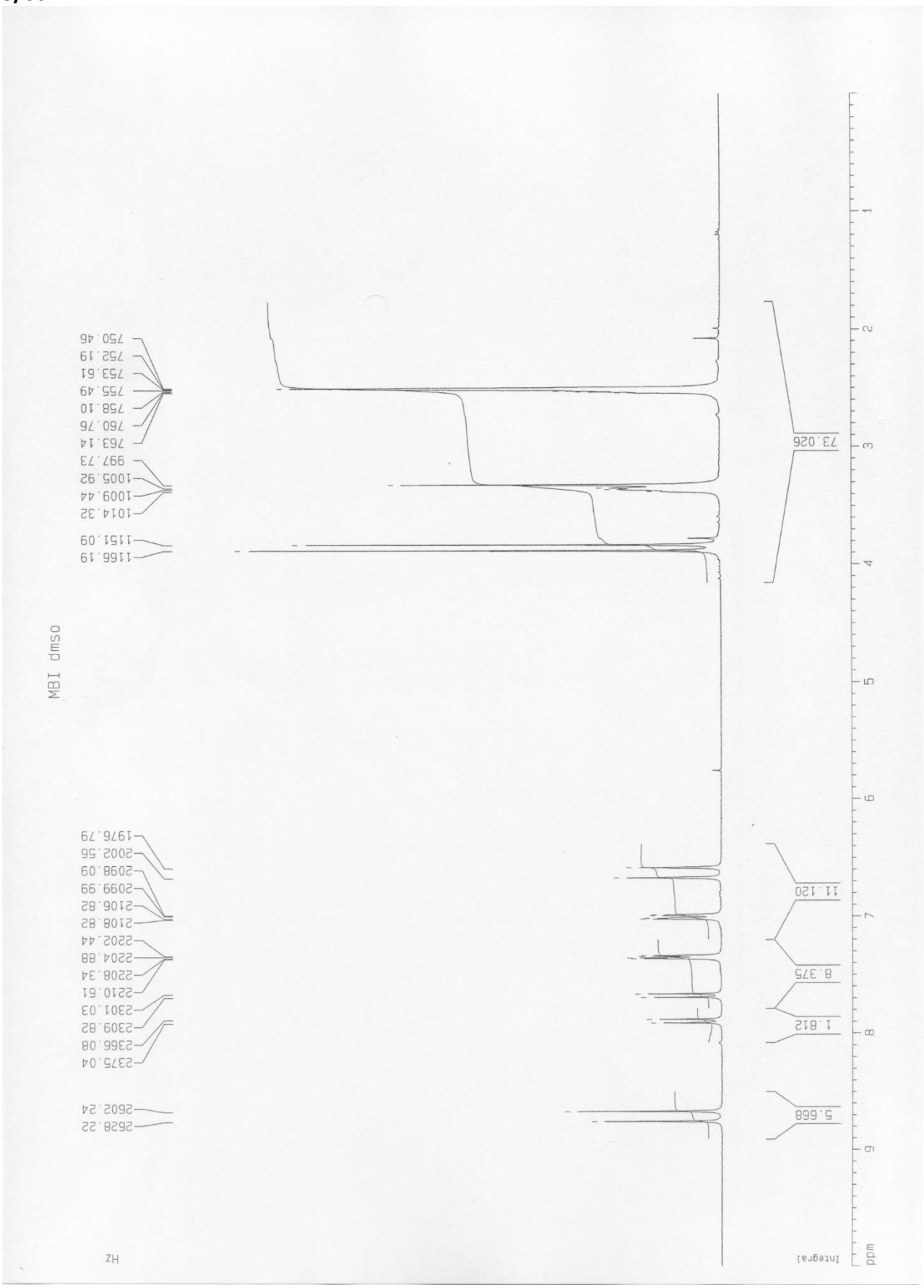

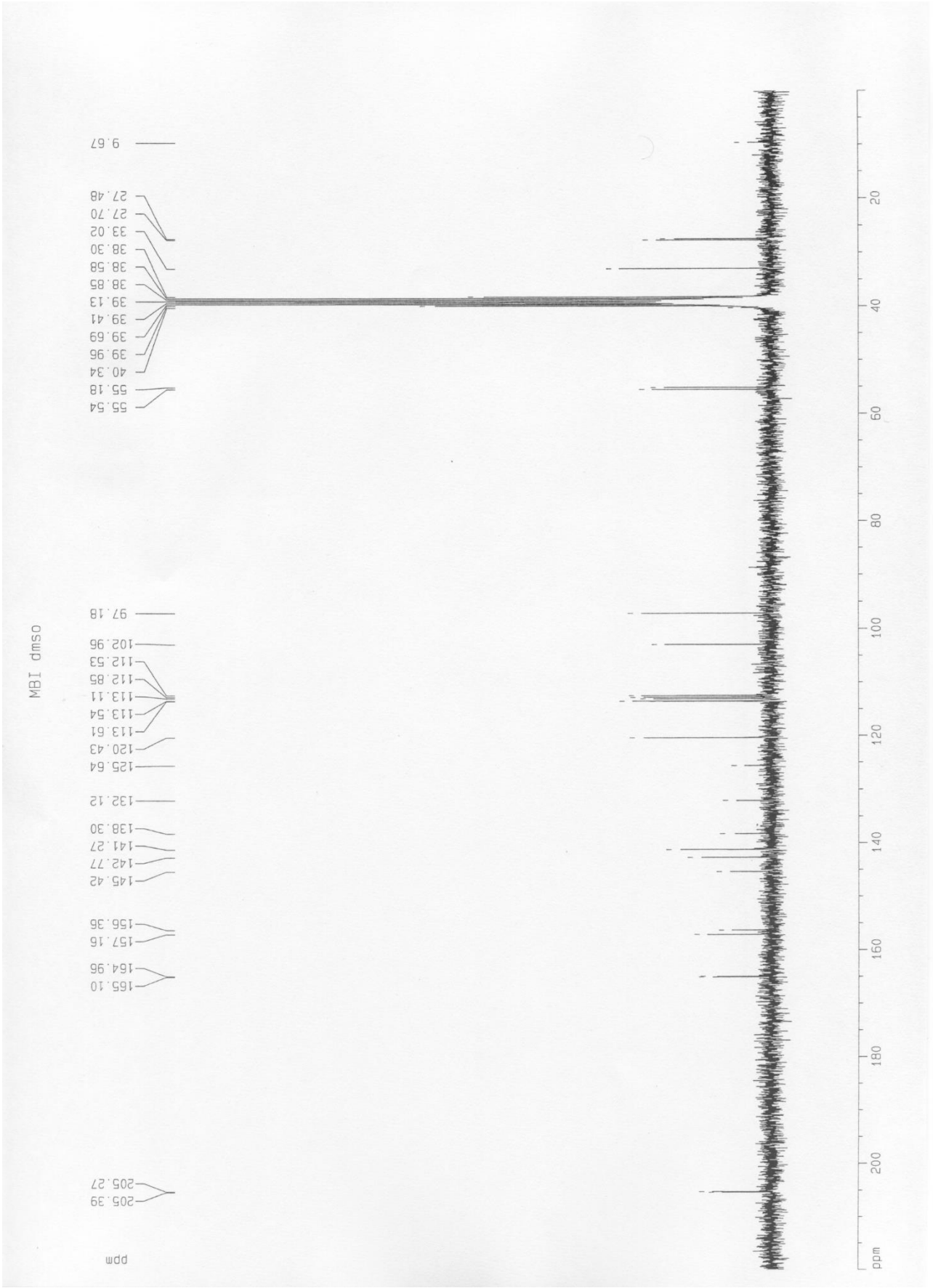

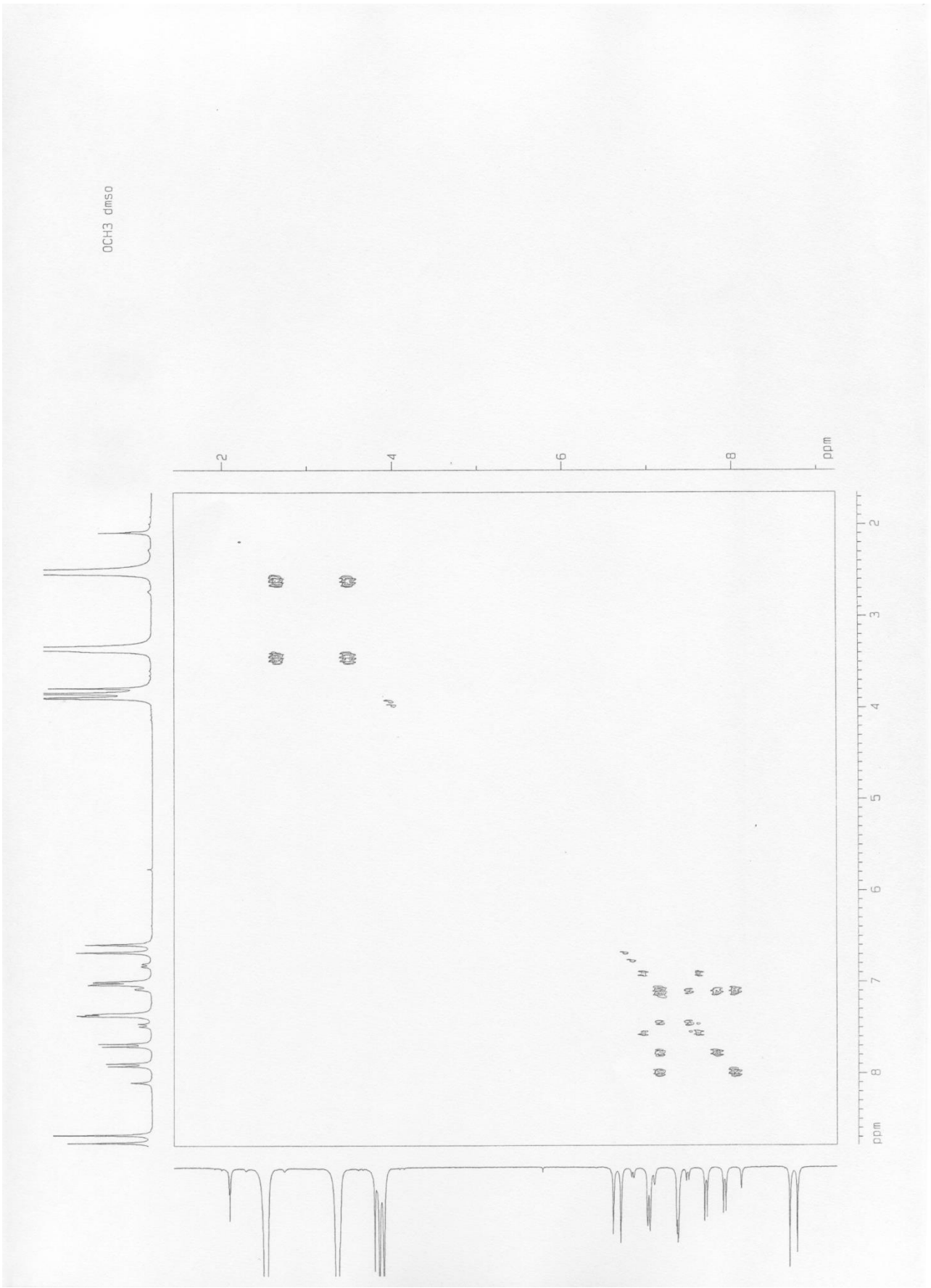

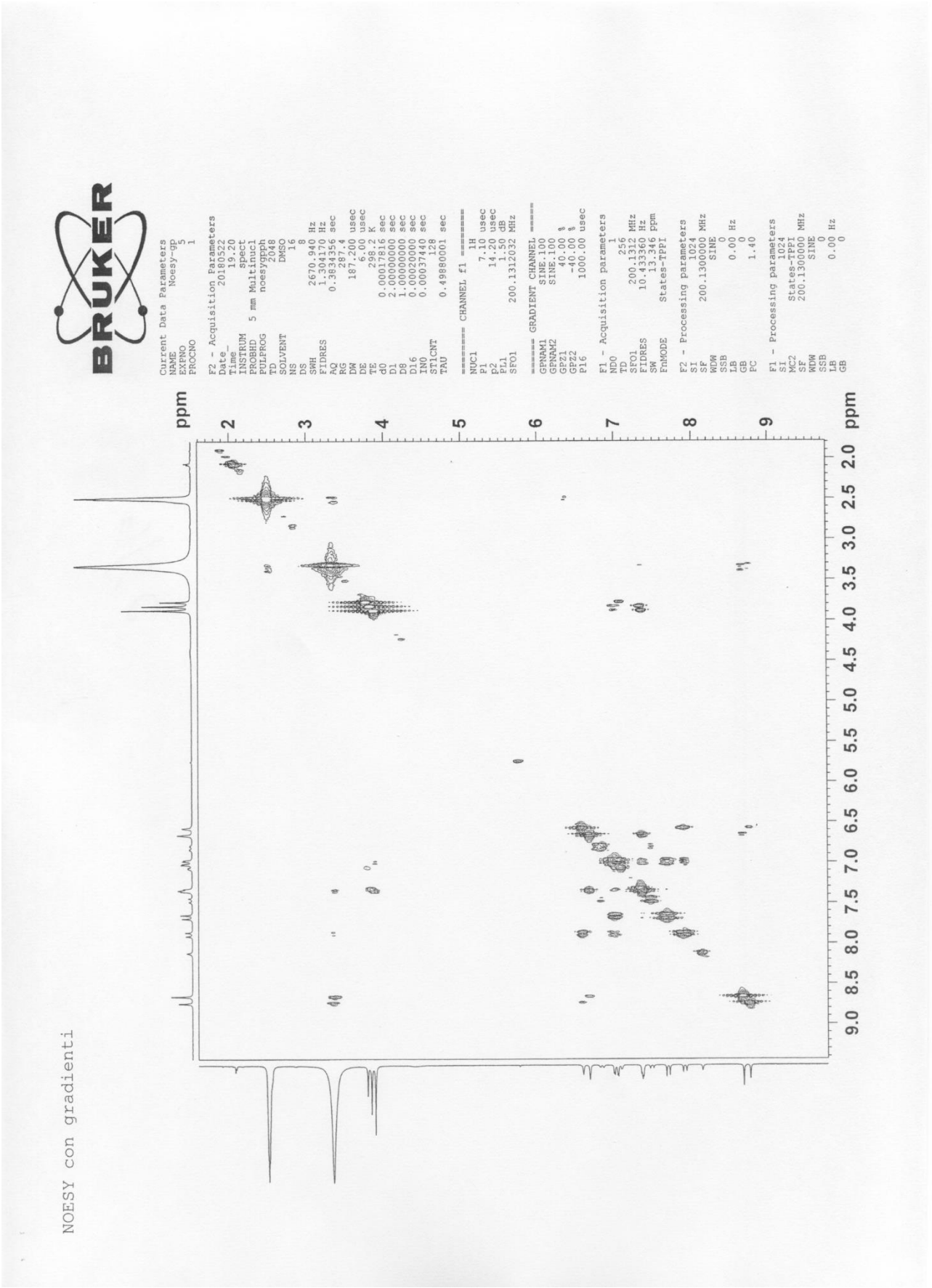

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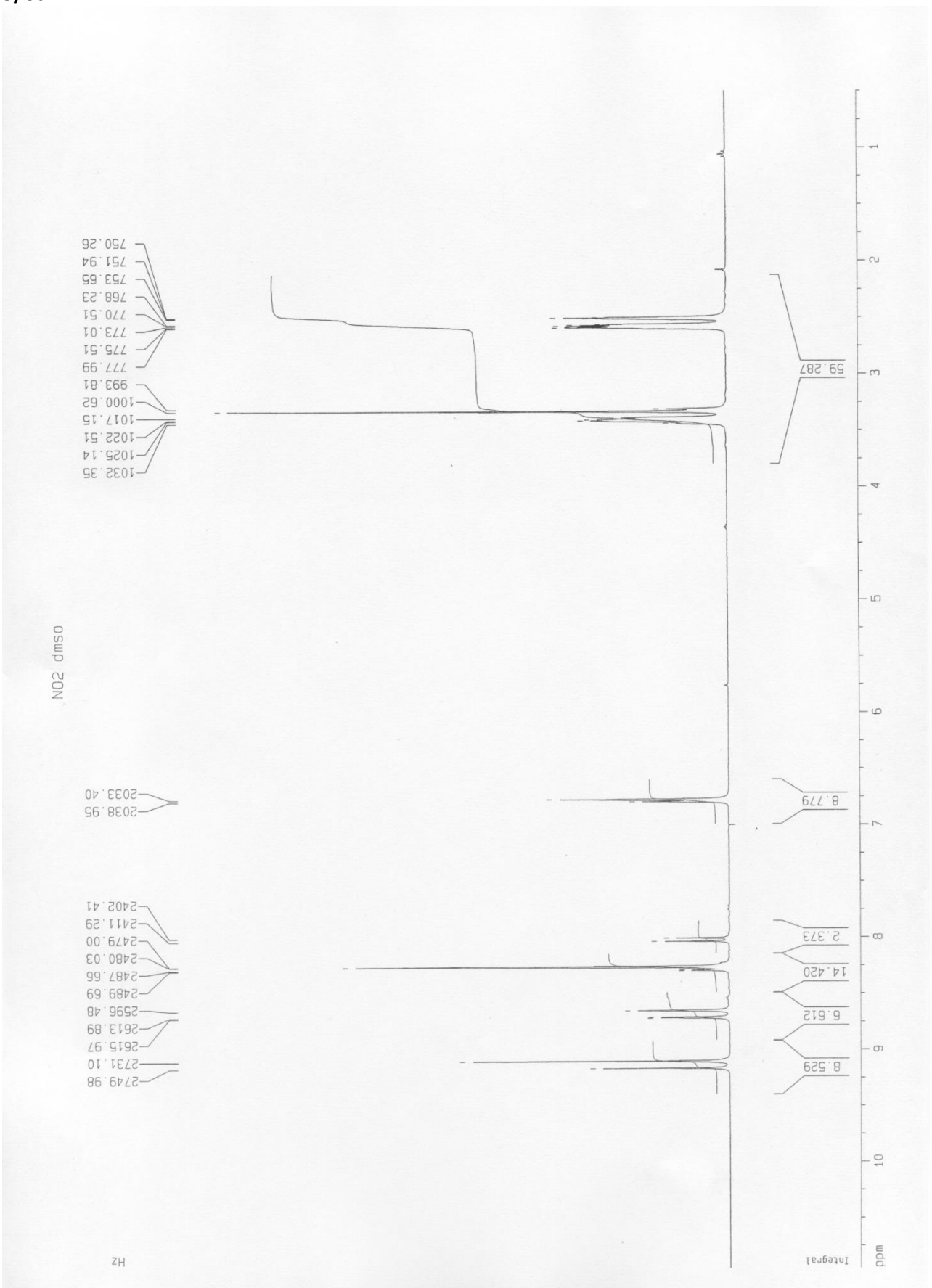

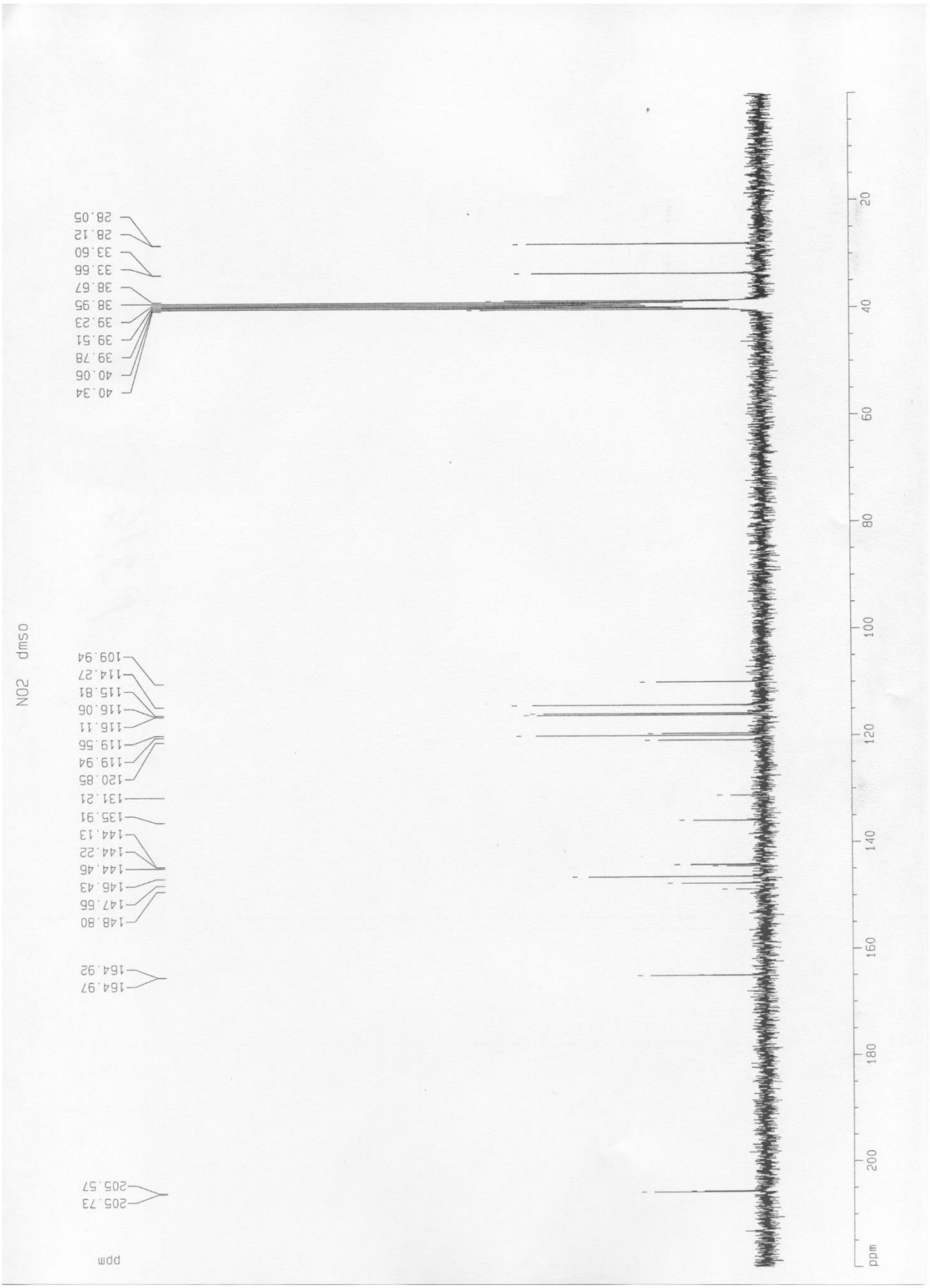

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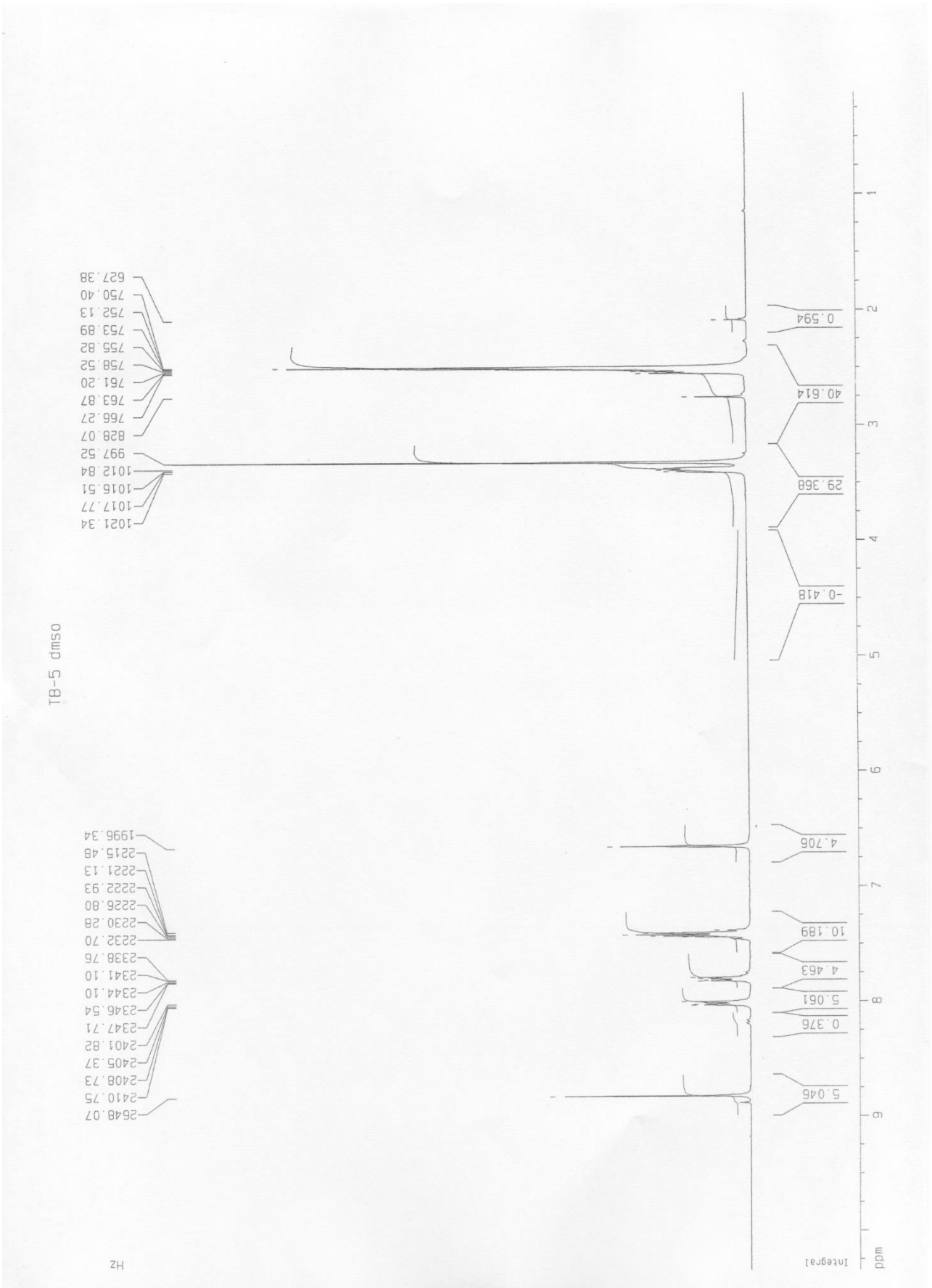

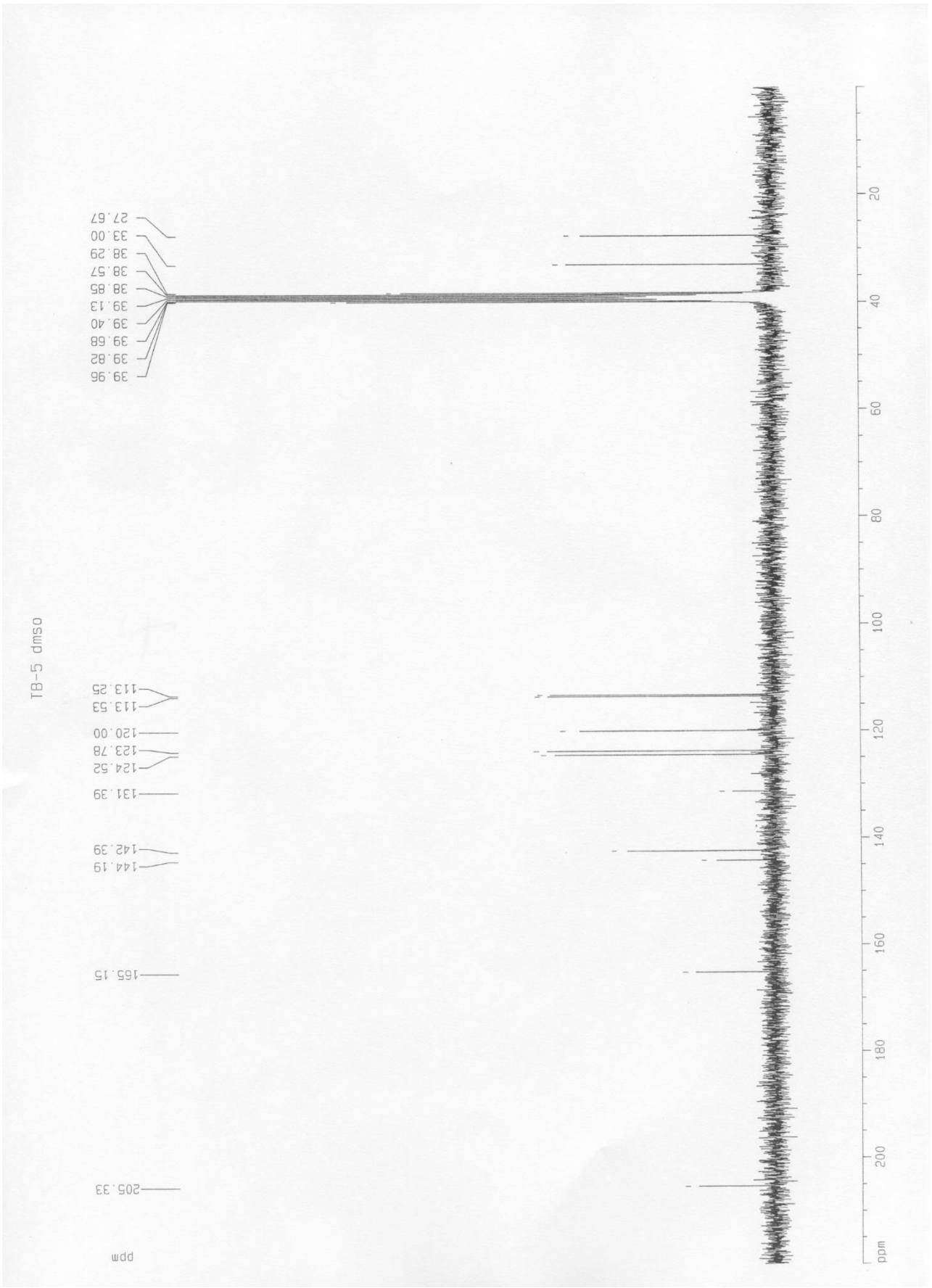

2. Primary antiviral activities of compounds 5a-d and 6a-d against IV/H1N1 and AD5.

Products **5**/**6a-d** were tested against the Herpesviridae family, Varicella-Zoster virus, (VZV, virus strain, Ellen, cell line, HFF), from the Hepatic virus HBV (virus strain ayw; cell line 2.2.15), Respiratory Viruses such as Influenza A virus H1N1 (IV/H1N1, virus strain, InfluenzaA/California/7/2009; cell line, MDCK), Adenovirus-5 (AD5, Adenoid75, virus strain; cell line, HFF), from the Togavidae family, Chikungunya virus (CV, virus strain, S27/VR-64, cell line, Vero 76), from the Flaviridae group, Yellow Fever Virus (YFV, virus strain, 17D; cell line, Huh7), from the Bunyaviridae family, Punta Toro Virus (PTV, virus strain, Adames; cell line, Vero 76), and from the Papovaviridae the Human Papilloma Virus (HPV, virus strain, HE611260.1; cell line, C-33A).

Table S1. Primary antiviral activities of compounds **5a-d** and **6a-d** against IV/H1N1 and AD5.

Entry	**5/6**	Drug Assay Name (Cytopathic eff.)	EC_{50}	CC_{50}	SI_{50}
		IV/H1N1[a]			
1	**a**	Visual	37	>100	>2.7
		Neutral Red	>100	>100	0
2	**b**	Visual	>100	>100	0
		Neutral Red	>100	>100	0
3	**c**	Visual	15	>100	>6.7
		Neutral Red	25	>100	>4.0
4	**d**	Visual	32	>100	>3.1
		Neutral Red	28	>100	>3.6
		Ribavirin[b]			
5		Visual	1.2	>320	>270
		Neutral Red	1.4	>320	>270
		AD5[c]			
6	**a**	CellTiter-Glo	>150	>150	1
7	**b**	CellTiter-Glo	>150	>150	1
8	**c**	CellTiter-Glo	>150	>150	1
9	**d**	CellTiter-Glo	>30	118.61	<4
		Cidofovir[d]			
10		CellTiter-Glo	2.93	121.85	42

[a]Drug conc. Range 0.1-100 □g/mL (vehicle, DMSO). [b]Control conc. Range 0.32-320 □g/mL. [c]Drug conc. Range 0.048-150 □M (vehicle, DMSO). [d]Control conc. Range 0.048-150 □M.

3. Cartesian Coordinates of calculated structures

5c*sin*

Input orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	2.593175	0.620494	0.256211
2	6	0	3.770523	-0.348907	0.156424
3	6	0	3.164143	-1.696012	-0.282643
4	6	0	1.692343	-1.412859	-0.431999
5	6	0	1.362402	-0.143171	-0.116140
6	1	0	4.277354	-0.397653	1.125969
7	1	0	4.498561	0.045935	-0.560310
8	1	0	3.589554	-2.058844	-1.227491
9	1	0	3.339772	-2.491404	0.453989
10	8	0	2.657219	1.794571	0.566708
11	7	0	0.094321	0.445333	-0.106795
12	6	0	-0.177526	1.805403	-0.280781
13	6	0	-1.156155	-0.178314	-0.002489
14	1	0	0.633890	2.511881	-0.368535
15	6	0	-2.094272	0.872499	-0.128328
16	6	0	-3.464535	0.605780	-0.052517
17	6	0	-1.552726	-1.498104	0.223870
18	6	0	-2.923196	-1.743677	0.299976
19	6	0	-3.866646	-0.710022	0.156977
20	1	0	-4.180960	1.415545	-0.149417
21	1	0	-3.267331	-2.758921	0.476633
22	1	0	-0.840835	-2.304135	0.361048
23	7	0	-1.446343	2.091402	-0.304683
24	1	0	0.996569	-2.169177	-0.775656
25	6	0	-5.890181	-1.492953	-1.087599
26	1	0	-6.978758	-1.735338	-1.024159
27	1	0	-5.755162	-0.692374	-1.855011
28	1	0	-5.349285	-2.405906	-1.436915
29	8	0	-5.367424	-1.043959	0.245022

5c*anti*

Input orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z

1	6	0	-2.803611	-0.607951	-1.153688
2	6	0	-4.115761	-1.281784	-0.753643
3	6	0	-4.171683	-1.204215	0.784388
4	6	0	-2.910592	-0.475249	1.167802
5	6	0	-2.137178	-0.159410	0.107505
6	1	0	-4.121939	-2.308133	-1.135682
7	1	0	-4.947619	-0.760040	-1.238861
8	1	0	-5.058639	-0.666535	1.144580
9	1	0	-4.210201	-2.198163	1.250019
10	8	0	-2.394714	-0.457952	-2.289366
11	7	0	-0.894717	0.479110	0.103706
12	6	0	-0.203825	0.932377	1.228020
13	6	0	-0.043102	0.726631	-0.984099
14	1	0	-0.658618	0.869772	2.204905
15	6	0	1.106605	1.313849	-0.417442
16	6	0	2.181380	1.718827	-1.219547
17	6	0	-0.162548	0.553155	-2.366202
18	6	0	0.903940	0.958675	-3.157606
19	6	0	2.069265	1.529118	-2.596219
20	1	0	3.051446	2.167604	-0.756709
21	1	0	0.864625	0.847864	-4.236315
22	1	0	-1.052875	0.141847	-2.827934
23	7	0	0.973517	1.423086	0.962615
24	1	0	-2.683654	-0.229100	2.198353
25	6	0	4.229984	2.451940	-3.018411
26	1	0	4.852185	2.638629	-3.895807
27	1	0	4.036238	3.401677	-2.501959
28	1	0	4.759674	1.774807	-2.334819
29	8	0	3.033044	1.869103	-3.505857

6c*sin*

Input orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	2.593175	0.620494	0.256211
2	6	0	3.770523	-0.348907	0.156424
3	6	0	3.164143	-1.696012	-0.282643
4	6	0	1.692343	-1.412859	-0.431999
5	6	0	1.362402	-0.143171	-0.116140
6	1	0	4.277354	-0.397653	1.125969

7	1	0	4.498561	0.045935	-0.560310
8	1	0	3.589554	-2.058844	-1.227491
9	1	0	3.339772	-2.491404	0.453989
10	8	0	2.657219	1.794571	0.566708
11	7	0	0.094321	0.445333	-0.106795
12	6	0	-0.177526	1.805403	-0.280781
13	6	0	-1.156155	-0.178314	-0.002489
14	1	0	0.633890	2.511881	-0.368535
15	6	0	-2.094272	0.872499	-0.128328
16	6	0	-3.464535	0.605780	-0.052517
17	6	0	-1.552726	-1.498104	0.223870
18	6	0	-2.923196	-1.743677	0.299976
19	6	0	-3.866646	-0.710022	0.156977
20	1	0	-4.180960	1.415545	-0.149417
21	1	0	-4.925343	-0.945592	0.219087
22	1	0	-3.267331	-2.758921	0.476633
23	7	0	-1.446343	2.091402	-0.304683
24	1	0	0.996569	-2.169177	-0.775656
25	6	0	-1.245438	-3.916023	0.785909
26	1	0	-0.512266	-4.746832	0.927292
27	1	0	-1.818174	-3.790548	1.736860
28	1	0	-1.962607	-4.216385	-0.016290
29	8	0	-0.541470	-2.643088	0.418734

6c*anti*

Input orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	-2.299520	-0.043743	-1.469034
2	6	0	-3.546635	0.801509	-1.206615
3	6	0	-3.462814	1.210461	0.277088
4	6	0	-2.168649	0.611821	0.760588
5	6	0	-1.535547	-0.105476	-0.187962
6	1	0	-4.437672	0.210651	-1.443621
7	1	0	-3.547003	1.659674	-1.887314
8	1	0	-3.463986	2.300009	0.413431
9	1	0	-4.311854	0.831563	0.861885
10	8	0	-1.990394	-0.552859	-2.529890
11	7	0	-0.328441	-0.817683	-0.093975
12	6	0	0.343567	-1.031783	1.107800

13	6	0	0.367849	-1.575945	-1.048296
14	1	0	0.009158	-0.538770	2.008174
15	6	0	1.412704	-2.197348	-0.326167
16	6	0	2.341536	-3.030710	-0.963049
17	6	0	0.259282	-1.736407	-2.442834
18	6	0	1.184091	-2.578388	-3.062278
19	6	0	2.205031	-3.215486	-2.329339
20	1	0	3.135858	-3.497779	-0.390854
21	1	0	2.902919	-3.854514	-2.863018
22	1	0	1.131225	-2.741662	-4.132157
23	7	0	1.362258	-1.835602	1.013946
24	1	0	-1.817056	0.733829	1.776597
25	6	0	-0.776925	-1.147357	-4.516585
26	1	0	-1.597942	-0.499998	-4.830763
27	1	0	0.158038	-0.798509	-4.972600
28	1	0	-0.978152	-2.175049	-4.845864
29	8	0	-0.727834	-1.051011	-3.100399

7*sin*

Input orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	-2.016442	-0.149210	-1.376841
2	6	0	-3.490203	-0.474353	-1.118020
3	6	0	-3.709297	-0.243744	0.391357
4	6	0	-2.392248	0.300272	0.877875
5	6	0	-1.450808	0.348835	-0.085753
6	1	0	-3.697733	-1.499887	-1.439019
7	1	0	-4.111451	0.182590	-1.737078
8	1	0	-4.524378	0.461409	0.598476
9	1	0	-3.969258	-1.171577	0.918650
10	8	0	-1.427285	-0.276926	-2.430918
11	7	0	-0.108952	0.716550	0.086755
12	6	0	0.811356	0.849314	-0.948804
13	6	0	0.618505	0.934479	1.265258
14	1	0	0.487626	0.752141	-1.977659
15	6	0	1.941792	1.178342	0.828672
16	6	0	2.958550	1.417820	1.760284
17	6	0	0.277365	0.907198	2.619175
18	6	0	1.304174	1.144656	3.529075
19	6	0	2.625169	1.396892	3.109557

20	1	0	3.972326	1.607430	1.421598
21	1	0	3.393180	1.578875	3.856194
22	1	0	1.075899	1.140721	4.591307
23	1	0	-0.739988	0.741457	2.950064
24	7	0	2.020785	1.127166	-0.560716
25	1	0	-2.238295	0.613993	1.906081

***7**anti*

Input orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	-2.150359	0.387127	1.158633
2	6	0	-3.252152	0.652696	0.138240
3	6	0	-2.763495	1.959538	-0.503690
4	6	0	-1.227959	1.785346	-0.510708
5	6	0	-0.873470	1.008531	0.559366
6	1	0	-4.238205	0.743500	0.543647
7	1	0	-3.252094	-0.149178	-0.570208
8	1	0	-3.201965	2.117037	-1.466933
9	1	0	-2.995711	2.799307	0.117409
10	8	0	-2.256943	-0.229625	2.250341
11	7	0	0.495293	0.802002	1.054071
12	6	0	1.415075	1.932557	0.767867
13	6	0	1.192068	-0.300130	0.398002
14	1	0	1.136022	2.962734	0.843793
15	6	0	2.462672	0.093069	0.104909
16	6	0	3.404299	-0.789830	-0.415958
17	6	0	0.720706	-1.570859	0.082100
18	6	0	1.633381	-2.486603	-0.481186
19	6	0	2.980247	-2.102298	-0.711145
20	1	0	4.413682	-0.481676	-0.592272
21	1	0	3.675417	-2.809608	-1.112832
22	1	0	1.310225	-3.474967	-0.733389
23	1	0	-0.296985	-1.845492	0.265893
24	7	0	2.608331	1.522066	0.401450
25	1	0	-0.553598	2.216653	-1.220716
